#411
4-23-01
M.L.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of Vilmos Kéri et al.

FWCIP of Serial No. 08/659,961

Filed on herewith

For PROCESS FOR THE ISOLATION AND PURUFUCATION, etc.

Attorney's Docket 0100-004

Hon. Commissioner of Patents and Trademarks
Washington DC 20231

Sir:

PRELIMINARY AMENDMENT

Prior to assigning a Serial No to the above-identified application, please amend it as follows:

In the disclosure

A1 Page 1, before line 1 insert --This is a continuation-in-part of application Ser. No.08/659,961 filed on June 7, 1996, which is a continuing application of Ser. No. 08/269,150 filed on June 30, 1994, both abandoned.--

A2 Page 3, line 5, after "Collection)" insert --and other bacterioal starins, such as *Aspergillus terreus*) acessible under ATCC 20542).--

Page 14, after the end of the page add the following new Examples:

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Example 7.

A3 cont 800 g fermentation liquor cultured by an *Aspergillus terreus* strain (deposition access No. ATTC 20542) containing a total amount of 630 mg of mevinolin both as lactone and as hydroxy acid were diluted to 1,200 g. with water. Then 2.4 g ethylene glycol were added to the mixture, and the pH was maintained at 9 to 9.5 by adding 20% wt. KOH solution under continuous stirring for

2 hours. The biomass was then filtered off and suspended in 400 cm^3 water. The suspension was adjusted to pH 9-9.5 with 20% wt. KOH solution, filtered again and the filtrates were combined. 1,480 cm^3 of filtered liquor containing 554 mg of active ingredient were obtained. Then 3.5 g of $CaCl_2$ were added to the liquor and the solution was adjusted to pH 2.1 with 15% wt. sulfuric acid solution under stirring. The separate precipitate was settled for 4 hours and processing was completed as in Example 2, with the difference that the active ingredient was dissolved from the precipitate with 120 cm^3 of isobutylacetate. 370 mg product was obtained. The obtained mevinolin has an active ingredient content of 98% by high pressure liquid chromatography, containing 0.2% dihydromevinolin by HPLC. $[\alpha]25_D7=+326°C$ (c=0.5; acetonitrile).

A3 cancld.

Example 8.

800 g of fermentation liquor cultured by an *Aspergillus terreus* strain and containing a total amount of 620 mg of mevinolin, both as a lactone and as hydroxy acid were diluted to 1200 g with water. Then 2.4 ethylene glycol were added to the mixture, and the pH was maintained at 8.5 to 9.0 by adding 20% wt. KOH solution under continuous stirring for 2 hours. The biomass was then filtered off and suspended in 400 cm^3 water containing 0.8 g of ethylene glycol. The suspension was adjusted to pH 8.5-9.0 with 20% wt. KOH solution, filtered again and the filtrates were combined. 1,470 cm^3 of filtered liquor containing 535 mg of the active ingredient were obtained which was adjusted to pH 3.0 with 15% wt. phosphoric acid under stirring. The precipitate was settled over 4 hours. The balance of the process was completed as described in Example 2, resulting in the isolation of 334 mg mevinolin with an active ingredient content of 98.6% by high pressure liquid chromatography, with a dihydromevinolin content of 0.2 % by HPLC. $[\alpha]25_D7=+328°C$ (c=0.5; acetonitrile).--

Respectfully submitted

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